## p63 Isoforms in epidermal morphogenesis

The transcription factor p63, which is expressed as isoforms that contain (TA) or lack (ΔN) a transactivation domain, is critical for epidermal morphogenesis. The precise function of ΔNp63 has remained elusive due, in part, to *in vitro* findings that suggest conflicting roles for this isoform in maintaining the proliferative potential of keratinocytes and regulating genes that promote terminal differentiation. Using an inducible epidermal-specific *ΔNp63* knockdown mouse model, Koster and colleagues recently provided *in vivo* evidence that ΔNp63 is critical for initiation of terminal differentiation pathways and for basement membrane integrity. Following knockdown of *ΔNp63*, the mice displayed severe skin fragility, an impaired ability to heal skin wounds, a failure of keratinocytes to exit the cell cycle or undergo terminal differentiation, and basement membrane abnormalities. Microarray studies revealed that ΔNp63 directly regulates distinct pathways involving Fras1, which is required for basement membrane integrity, and IκB-kinase-α, which is important at later stages of epidermal morphogenesis. (*Proc Natl Acad Sci USA* 104:3255–60, 2007)

## More filaggrin mutations

Two prevalent null alleles of the gene encoding filaggrin (*FLG*), a protein essential for epidermal barrier formation and hydration, were identified in icthyosis vulgaris patients with a high incidence of atopic dermatitis (AD). Sandilands and colleagues reported a complex strategy for the comprehensive sequence analysis of this highly repetitive and problematic gene. Fifteen additional nonsense or frameshift mutations were identified. Of these mutations, five were prevalent in Irish population controls and were significantly associated with an increased risk of AD. The discovery of three additional uncommon mutations in Irish subjects suggests that the genetic architecture of AD may consist of recurrent risk alleles as well as individual rare or private risk alleles. Notably, this comprehensive assessment strategy will allow efficient and in-depth screening of additional cohorts for mutations in *FLG*. (*Nat Genet* 39:650–4, 2007)

## The reality of hair regeneration

Despite contrary findings published a half century ago, the central dogma in cutaneous biology asserts that hair follicles form only during development; thus, adult hair-follicle loss is considered permanent. *De novo* hair-follicle regeneration, however, was recently reported by Ito and colleagues in mice following wounding-induced re-epithelialization. Genetic labeling experiments revealed that cells from the hair bulge contributed to re-epithelialization but that new hair follicles arise from cells outside the hair-follicle stem cell niche. This *de novo* formation of hair follicles following wounding recapitulates embryogenesis with respect to molecular markers and establishment of a stem cell compartment. Furthermore, this hair-follicle neogenesis is dependent on Wnt signaling because induced expression of a Wnt inhibitor abrogated generation of new hair follicles and overexpression of the secreted ligand Wnt7a resulted in twice the number of developing hair follicles. These exciting results suggest that modulation of the Wnt pathway may be utilized to decrease scar formation and stimulate hair regrowth. (*Nature* 447:316–20, 2007)

## Sunburn nation

Episodic acute overexposure to ultraviolet radiation (sunburn) increases the risk of both basal-cell carcinoma and melanoma. The Centers for Disease Control and Prevention analyzed cross-sectional data from the 1999, 2003, and 2004 Behavioral Risk Factor Surveillance System in an effort to monitor sunburn prevalence. The telephone surveys assessed the occurrence of sunburns during the preceding 12 months as well as information about race, ethnicity, gender, and age. Sunburn prevalence among all adults increased from 31.8% in 1999 to 33.7% in 2004. In addition, approximately two-thirds of these adults reported multiple sunburns in this time frame. Men consistently had a higher prevalence of sunburn than women, and increases were noted for both white women and white men from 1999 to 2004. In addition, sunburn was prevalent among racial/ethnic groups traditionally considered at low risk for sunburn and skin cancer. These results strongly support additional research to develop successful public health interventions to improve sun protection behaviors in all racial/ethnic groups. *Morb Mortal Wkly Rep* 56:524–8, 2007)

## Understanding glucocorticoids

Although glucocorticoids (GCs) are commonly used to treat contact dermatitis, their target cells and modes of action are unclear. Using a contact hypersensitivity (CHS) model of human allergic contact dermatitis, Tuckermann and colleagues demonstrated that the challenge phase, which involves reintroduction to the hapten, and not the sensitization phase, which involves the initial exposure and immunological response, is responsive to GCs. Selective deletion of the GC receptor (GR) in keratinocytes, T cells, and myeloid cells revealed that neutrophils and macrophages require GR function for suppression of CHS by GC. In addition, the impaired downregulation of several cytokines and chemokines (interleukin-1β, monocyte chemoattractant protein-1, macrophage inflammatory protein-2, and interferon-γ-inducible protein 10) following GC treatment in the mutant GR mice suggests that a network of inflammatory mediators is affected by the GR dimer. Overall, these findings offer promising alternative targets treatment of contact dermatitis. (*J Clin Invest* 117:1381–90, 2007)

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